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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	10

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/917,154	Applicant(s) Monahan et al.
	Examiner William Sandals	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 19, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) *19 and 20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jul 27, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Claims 19 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 9, mailed December 19, 2002.

2. Applicant's election without traverse of Group I, claims 1-18 in Paper No. 9 is acknowledged.

3. Claims 1-20 are pending in the application, claims 19-20 are withdrawn from examination. The restriction requirement is hereby made final.

Priority

4. It is noted that this application appears to claim subject matter disclosed in prior copending Application No. 08/571,536, filed December 13, 1995. A reference to the US patent issued from Application No. 08/571,536 is set forth in the priority claim filed on October 8, 2001, however, the application number has not been mentioned. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Priority for the independent claims 1 and 8 is supported in US Application No. 08/571,536.

Drawings

5. The drawings as submitted on July 27, 2001, have been approved by the draftsman.

Specification

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the sequence rules, 37 CFR 1.821 - 1.825. Sequences appear in the specification at pages 45, 49 and 54 for instance. All occurrences of sequences in the specification must be accompanied by a sequence number identifier. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). An amendment to the specification, a sequence listing, and a computer readable file is required in the reply to this office action. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Rejections - 35 USC § 112

7.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 5, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 5 recites the limitation "the time period" in line 2. There is insufficient antecedent basis for this limitation in the claim.

10. Claims 16 and 17 recite that they depend from claims 1 and 8. The use of the word "and" in this recitation is vague and indefinite since the relationship of claims 1 and 8 is thereby put into question. Does claim 1 depend from claim 8 and is the subject matter of claim 1 contained in claim 8, and vice versa? The claims should be amended to recite that the claims depend from claims 1 **or** 8.

11. Claim 17 recites the limitation "the extravascular parenchymal space" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 8-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-14 of U.S. Patent No. 6,379,966. Although the conflicting claims are not identical, they are not patentably distinct from each other because independent claims 1 and 11 of US 6,379,966 are a sub-genus of the instant claim 8. The dependent claims 2-10 and 12-13 of US 6,379,966 repeat the claimed subject matter of the instant dependent claims 9-15.

14. Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7, 9, 11 and 12 of copending Application No. 09/391,260. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 1-7 are generic to the sub-genus of claims 7, 9, 11 and 12 of copending Application No. 09/391,260.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 1-7, 17 and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20 and 22 of copending Application No. 09/447,966. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 1-7 are generic to the sub-genus of claims 19, 20 and 22 of copending Application No. 09/447,966.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 and 37-39 of copending Application No. 09/707,000. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 1-7 are generic to the sub-genus of claims 1-15 and 37-39 of copending Application No. 09/707,000.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

18. Claims 1-5, 7-13, 15 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,328,470 (Nabel et al., (A)).

Nabel et al. (A) teach at the abstract, column 4, line 43 bridging to column 5, line 49, column 7, lines 19-51, column 8, lines 32-35, and lines 51-68, column 12, line 62 bridging to column 15, line 4, a process for delivering a polynucleotide into an extravascular parenchymal cell of a mammal by inserting the polynucleotide into a mammalian blood vessel in-vivo, increasing the permeability of the blood vessel, passing the polynucleotide in a solution through the blood vessel into the extravascular space, thereby delivering the polynucleotide into an extravascular parenchymal cell, and then expressing the polynucleotide. The permeability of the blood vessel is increased with pressure against the blood vessel walls, which may be done by

increasing the volume of the fluid in the blood vessel. The time of residence of the polynucleotide-containing solution in the blood vessel and pressure are variable. Various tissues may be treated by this process, including the liver (hepatocytes). Instant claim 8 recites that the polynucleotide alone has a more negative zeta potential than a polynucleotide-compound complex. Polynucleotides are well known to those of ordinary skill in the art to have a negative zeta potential. The polynucleotide-liposome complex taught by Nabel et al. (A) is known to have a less negative zeta potential than the polynucleotide alone. Therefore, the teachings of Nabel et al. (A) anticipate the instant claimed invention.

19. Claims 1-5, 7-13, 15 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,698,531 (Nabel et al., (B)).

Nabel et al. (B) teach at the abstract, column 3, line 52 bridging to column 4, line 24, column 5, line 54 bridging to column, column 7, line 50, column 9, lines 57-67, column 10, lines 41-53, and column 11, lines 19-37, a process for delivering a polynucleotide into an extravascular parenchymal cell of a mammal by inserting the polynucleotide into a mammalian blood vessel in-vivo, increasing the permeability of the blood vessel, passing the polynucleotide in a solution through the blood vessel into the extravascular space, thereby delivering the polynucleotide into an extravascular parenchymal cell, and then expressing the polynucleotide. The permeability of the blood vessel is increased with pressure against the blood vessel walls, which may be done by increasing the volume of the fluid in the blood vessel. The time of

residence of the polynucleotide-containing solution in the blood vessel and pressure are variable. Various tissues may be treated by this process, including the liver (hepatocytes). Instant claim 8 recites that the polynucleotide alone has a more negative zeta potential than a polynucleotide-compound complex. Polynucleotides are well known to those of ordinary skill in the art to have a negative zeta potential. The polynucleotide-liposome complex taught by Nabel et al. (B) is known to have a less negative zeta potential than the polynucleotide alone. Therefore, the teachings of Nabel et al. (B) anticipate the instant claimed invention.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of US 5,328,470 (Nabel et al., (A)) and US 5,698,531 (Nabel et al., (B)) in view of US 5,026,558 (Hwang).

The claims are drawn to a process for delivering a polynucleotide into an extravascular parenchymal cell of a mammal by inserting the polynucleotide into a mammalian blood vessel in-vivo, increasing the permeability of the blood vessel, passing the polynucleotide in a solution through the blood vessel into the extravascular space, thereby delivering the polynucleotide into

the extravascular parenchymal cell, and then expressing the polynucleotide. The permeability of the blood vessel is increased with pressure against the blood vessel walls, which may be done by increasing the volume of the fluid in the blood vessel. The time of residence of the polynucleotide-containing solution in the blood vessel and pressure are variable. Various tissues may be treated by this process, including the liver (hepatocytes). Instant claim 8 recites that the polynucleotide alone has a more negative zeta potential than a polynucleotide-compound complex. The blood vessel may be a tail vein as recited in claims 6 and 14. The volume of the solution my be at least milliliter, claim 16. The pressure in the extravascular parenchymal space may be at least 10 mm mercury, claim 18.

Each of Nabel et al., (A) and Nabel et al., (B) teach the invention as described above in the rejection under 35 USC 102. Each of Nabel et al., (A) and Nabel et al., (B) teach the delivery of the polynucleotide to the blood vessel with a catheter, applying pressure to the solution in the catheter to force the polynucleotide out of the blood vessel into the parenchymal space.

Each of Nabel et al., (A) and Nabel et al., (B) did not teach the blood vessel may be a tail vein, nor that the volume of the solution may be at least one milliliter, nor that the pressure in the extravascular parenchymal space may be at least 10 mm mercury.

Hwang teaches at example 2, the delivery of a polynucleotide by injection into a tail vein, and also to a blood vessel with a catheter, for transfecting the parenchymal cells of the liver.

The limitations of instant claim 16, delivery solution volume of at least one milliliter, and instant claim 18, the pressure in the extravascular parenchymal space may be at least 10 mm

mercury, are routine parameters which are well known to those of skill in the art, and in the absence of unexpected results, do not provide patentable distinction for the instant claimed invention.

It would have been prima facie obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of each of Nabel et al., (A) and Nabel et al., (B) with Hwang to produce the instant claimed invention because each of Nabel et al., (A), Nabel et al., (B) and Hwang teach a method of delivery of a polynucleotide to parenchymal cells via a blood vessel, and expressing the polynucleotide. The teachings of Hwang make obvious the modification of the method to administer the polynucleotide via a tail vein.

One of ordinary skill in the art would have been motivated to combine the teachings of each of Nabel et al., (A) and Nabel et al., (B) with Hwang to produce the instant claimed invention because Hwang teaches the desirable and beneficial delivery of a polynucleotide to a parenchymal cell via a blood vessel via a blood vessel which may be in the alternative, delivery by injection into a tail vein or by delivery to a blood vessel using a catheter. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Nabel et al., (A), Nabel et al., (B) and Hwang.

Conclusion

22. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61

(November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.
Examiner
March 5, 2003

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Applicat[redacted] No. 09/917154

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

☑ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821 - 1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

☑ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

☑ 7. Other: Sequences appear in the specification without Sequence Ident. Fig.

Applicant must provide:

☑ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"

☑ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification

☑ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308-1123
For CRF submission help, call (703) 308-4212
For PatentIn software help, call (703) 557-0400

Please return a copy of this notice with your response.